

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

Please add claims 60-73.

1. **(Currently amended)** A pharmaceutical composition that provides an elastin-based composition for localized delivery in vivo, said elastin-based composition comprising a polypeptide, wherein said polypeptide comprises (i) an amino acid sequence at least 90% 80% identical to SEQ ID NO: 3, ~~or~~ (ii) a bioactive fragment of SEQ ID NO: 3 that includes one to seven repeats of a ~~(ii) a peptide fragment including at least one~~ hexameric sequence represented by SEQ ID NO: 1, or (iii) a peptide fragment consisting essentially of one to seven repeats of the hexameric sequence represented by SEQ ID NO: 1, wherein said elastin-based composition is attached to a biocompatible support or dissolved in a biocompatible matrix and has one or more biological activities selected from the group consisting of:

- a) inhibiting the proliferation of smooth muscle cells in vivo;
- b) stimulating the differentiation of smooth muscle cells in vivo;
- c) regulating the migration of smooth muscle cells in vivo; and
- d) binding to smooth muscle cells, and

wherein said elastin-based composition has an IC50/EC50 for at least one of said biological activities that is less than or equal to 10^{-3} .

2. **(Original)** The pharmaceutical composition of claim 1 wherein said elastin-based composition is soluble and has an IC50/EC50 for each of said one or more biological activities that is less than or approximately equal to 10^{-3} .

3. **(Previously presented)** The composition of claim 1 or 2 wherein said IC50/EC50 is greater than 10^{-15} .

4. **(Original)** The composition of claim 1 wherein said pharmaceutical composition provides a dose of said elastin-based composition equivalent to 10^{-8} M of a peptide having the amino acid sequence of SEQ ID NO:2 at said target site.

5. **(Withdrawn)** The composition of claim 1 wherein said pharmaceutical composition comprises an expression vector encoding a tropoelastin or a fragment thereof.
6. **(Previously presented)** The composition of claim 1 wherein said elastin-based composition comprises a recombinant polypeptide.
7. **(Previously presented)** The composition of claim 1 wherein said elastin-based composition comprises a synthetic peptide.
8. **(Previously presented)** The composition of claim 7 wherein said synthetic peptide comprises at least two repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).
9. **(Previously presented)** The composition of claim 8 wherein said synthetic peptide comprises 6 repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).
10. **(Original)** The composition of claim 1, wherein said elastin-based composition is crosslinked, precipitated, or coacervated.
11. **(Original)** The composition of claim 1 wherein said elastin-based composition comprises an elastin matrix produced from a blood vessel.
12. **(Previously presented)** The composition of claim 1 wherein said elastin-based composition is attached to a biocompatible support or biocompatible matrix.
13. **(Previously presented)** The composition of claim 12 wherein said biocompatible support or biocompatible matrix comprises a tube.

14. **(Previously presented)** The composition of claim 13 wherein said elastin-based composition is attached to an outer surface of said tube and additionally comprises a sheath encircling said tube.
15. **(Withdrawn)** A method for producing an elastin-based composition according to claim 11 comprising:
- a) removing adventitia from a blood vessel;
 - b) treating said blood vessel with an ionic denaturing detergent solution;
 - c) after detergent treatment, treating said blood vessel with an alkaline solution; and
 - d) after alkaline treatment, removing residual adventitia, if any, from said blood vessel to produce an elastin-containing matrix;
 - e) removing residual collagen from said elastin-containing matrix to produce an elastin matrix.
16. **(Withdrawn)** The method of claim 15 wherein said detergent solution comprises sodium dodecyl sulfate.
17. **(Withdrawn)** The method of claim 15 wherein said detergent solution comprises between about 0.1 and 10% detergent.
18. **(Withdrawn)** The method of claim 15 wherein said alkaline solution comprises potassium hydroxide.
19. **(Withdrawn)** The method of claim 15 wherein said alkaline solution comprises about 0.1 to about 6 N base.
20. **(Withdrawn)** A method for preparing a biocompatible support comprising an elastin-based composition, said method comprising:
- a) rehydrating the elastin matrix of claim 11;
 - b) mounting said elastin matrix on a biocompatible support; and
 - c) drying the elastin matrix/support assembly.

21. **(Withdrawn)** The method of claim 19 wherein the elastin matrix/support assembly is tubular, additionally comprising inserting the tubular elastin matrix/support assembly into a tubular sheath so that the elastin matrix is sandwiched between the support and the sheath.
22. **(Previously presented)** A method for prophylaxis or treatment of a disorder having diminished capacity to regulate smooth muscle cell function comprising delivery of the elastin-based composition provided by the pharmaceutical composition of claim 1 to said site of diminished capacity to regulate smooth muscle cell function.
23. **(Previously presented)** The method of claim 22 wherein said IC₅₀/EC₅₀ is greater than about 10⁻¹⁵.
24. **(Original)** The method of claim 22 wherein said pharmaceutical composition provides a dose of said elastin-based composition equivalent to 10⁻⁸ M of a peptide having the amino acid sequence of SEQ ID NO:2 at said target site.
25. **(Withdrawn)** The method of claim 22 wherein said pharmaceutical composition comprises an expression vector encoding a tropoelastin or a fragment thereof.
26. **(Previously presented)** The method of claim 22 wherein said elastin-based composition comprises a recombinant polypeptide.
27. **(Previously presented)** The method of claim 22 wherein said elastin-based composition comprises a synthetic peptide comprising 6 repeats of the hexameric sequence Val-Gly-Val-Ala-Pro-Gly (SEQ ID NO: 1).
28. **(Original)** The method of claim 22 wherein said elastin-based composition is crosslinked, precipitated, or coacervated.

29. **(Original)** The method of claim 22 wherein said elastin-based composition comprises an elastin matrix produced from a blood vessel.
30. **(Previously presented)** The method of claim 22, wherein said elastin-based composition is attached to a biocompatible support or a biocompatible matrix.
31. **(Previously presented)** The method of claim 30 wherein said biocompatible support or biocompatible matrix comprises a tube.
32. **(Original)** The method of claim 22 wherein said target site is located in the cardiovascular system and is suspected or known to be at risk for disease.
33. **(Original)** The method of claim 22 wherein delivery comprises intravascular delivery of said elastin-based composition directly to a vascular site.
34. **(Original)** The method of claim 33 wherein said disorder is selected from the group consisting of atherosclerosis, restenosis, vascular bypass graft stenosis, transplant arteriopathy, aneurysm, and dissection.
35. **(Original)** The method of claim 22 wherein said elastin-based composition is delivered to and maintained at said site.
36. **(Previously presented)** The method of claim 35 wherein said pharmaceutical composition is a tubular elastin-based composition and said method comprises using said pharmaceutical composition as a blood vessel.
37. **(Previously presented)** The method of claim 36 wherein said blood vessel is used for vascular bypass.
38. **(Previously presented)** The method of claim 37 wherein said blood vessel is used for coronary artery bypass grafting.

39. **(Previously presented)** A method comprising implanting the pharmaceutical composition of claim 1 at a target site, wherein said target site is selected from the group consisting of the common bile duct, a pancreatic duct, the esophagus, the urethra, the bladder, the uterus, and an ovarian duct.
40. **(Withdrawn)** A method for prophylaxis or treatment of a disorder characterized by diminished capacity to regulate smooth muscle cell function comprising administering an elastase inhibitor to an individual known or suspected to have such a disorder.
41. **(Withdrawn)** The method of claim 40 wherein said individual has only one functional elastin gene.
42. **(Withdrawn)** The method of claim 40 wherein said disorder comprises SVAS or hypertension.
43. **(Withdrawn)** A method to screen for a drug candidate useful in the prophylaxis or treatment of a disorder characterized by a diminished capacity to regulate smooth muscle cell function comprising administering a drug to an ELN +/- or ELN -/- organism or cell and determining whether said drug:
- a) increases elastin mRNA or protein levels or elastin activity in said ELN +/- organism or cell;
 - b) inhibits smooth muscle cell proliferation, stimulates smooth muscle cell differentiation, or regulates vascular smooth muscle cell migration;
 - c) inhibits occlusion of arteries in said organism; and/or
 - d) lengthens the lifespan of said ELN -/- organism.
44. **(Withdrawn)** The method of claim 43 wherein said disorder comprises atherosclerosis, SVAS, or hypertension, and said method comprises measuring synthesis of elastin RNA in the presence of said drug as an indication of said drug's capacity to increase elastin mRNA levels.

45. **(Withdrawn)** The method of claim 43 wherein said disorder comprises atherosclerosis, SVAS, or hypertension, and said method comprises measuring synthesis of elastin protein in the presence of said drug as an indication of said drug's capacity to increase elastin protein levels.

46. **(Withdrawn)** The method of claim 43 wherein said disorder comprises atherosclerosis, SVAS, or hypertension, and said method comprises measuring activity of elastase in the presence of said drug as an indication of said drug's capacity to increase elastin protein levels.

47. **(Withdrawn)** The method of claim 43 wherein said disorder comprises atherosclerosis, transplant arteriopathy, or restenosis, and said method comprises treating and ELN -/- organism or an ELN -/- cell with said drug and measuring inhibition of vascular smooth muscle cell proliferation, stimulation of vascular smooth muscle cell differentiation, or regulation of vascular smooth muscle cell migration.

48. **(Currently amended)** The pharmaceutical composition of claim 1, wherein said elastin-based composition comprises a polypeptide comprising (i) an amino acid sequence at least 95% 90% identical to SEQ ID NO: 3, or (ii) a bioactive fragment of SEQ ID NO: 3 that includes one to seven repeats of a (ii) a peptide fragment including at least one hexameric sequence represented by SEQ ID NO: 1, or (iii) a peptide fragment consisting essentially of one to seven repeats of the hexameric sequence represented by SEQ ID NO: 1, wherein said elastin-based composition is attached to a biocompatible support or dissolved in a biocompatible matrix and has one or more biological activities selected from the group consisting of:

- a) inhibiting the proliferation of smooth muscle cells in vivo;
- b) stimulating the differentiation of smooth muscle cells in vivo;
- c) regulating the migration of smooth muscle cells in vivo; and
- d) binding to smooth muscle cells, and

wherein said elastin-based composition has an IC₅₀/EC₅₀ for at least one of said biological activities that is less than or equal to 10⁻³.

49. **(Currently amended)** The pharmaceutical composition of claim 48, wherein said peptide fragment consists essentially of three to six repeats of the elastin-based composition

~~comprises a polypeptide comprising (i) an amino acid sequence identical to SEQ ID NO: 2, or (ii) an amino acid sequence identical to SEQ ID NO: 3, or (iii) a peptide fragment including at least one hexameric sequence represented by SEQ ID NO: 1.~~

50. **(Previously presented)** The pharmaceutical composition of claim 1, wherein said elastin-based composition is derivatized by linkage to one or more additional chemical groups for promoting sustained release.

51. **(Previously presented)** A method for prophylaxis or treatment of obstructive vascular disease, comprising delivering an amount of the elastin-based composition of claim 1 effective to inhibit or decrease obstruction of a vessel, wherein said elastin-based composition is delivered to the site of vessel obstruction.

52. **(Previously presented)** A method for prophylaxis or treatment of vascular stenosis, comprising delivering an amount of the elastin-based composition of claim 1 effective to inhibit or decrease vascular stenosis, wherein said elastin-based composition is delivered to the site of vascular stenosis.

53. **(Previously presented)** A method for prophylaxis or treatment of stenosis, comprising delivering an amount of the elastin-based composition of claim 1 effective to inhibit or decrease stenosis, wherein said elastin-based composition is delivered to the site of stenosis, and wherein said site is selected from the group consisting of common bile duct, pancreatic duct, esophagus, urethra, bladder, uterus, and ovarian duct.

54. **(Previously presented)** A method for decreasing restenosis following angioplasty or bypass grafting, comprising delivering an amount of the elastin-based composition of claim 1 effective to decrease restenosis following angioplasty or bypass grafting, wherein said elastin-based composition is delivered to the site of restenosis.

55. **(Previously presented)** The composition of claim 1, wherein the elastin-based composition is a hexapeptide having the sequence represented in SEQ ID No: 1.

56. **(Previously presented)** The composition of any of claims 1, 2, 8, 9 or 55, where said elastin-based composition is dissolved or suspended within a biocompatible polymer matrix, which matrix permits diffusion of the elastin-based composition, to form a sustained-release composition.

57. **(Previously presented)** The composition of claim 56, wherein the biocompatible polymer matrix is selected from the group consisting of polyester, a polylactide, degradable lactic acid-glycolic acid copolymers, and poly-D-(-) hydroxybutyric acid.

58. **(Previously presented)** The composition of claim 56, wherein the biocompatible polymer matrix is formulated for coating an implantable medical device.

59. **(Previously presented)** The composition of claim 56, wherein the biocompatible polymer matrix is formulated for coating a stent.

Please add the following claims:

60. **(New)** A pharmaceutical composition that provides an elastin-based composition, said elastin-based composition comprising a polypeptide, wherein said polypeptide consists essentially of (i) an amino acid sequence at least 90% identical to SEQ ID NO: 3, (ii) a bioactive fragment of SEQ ID NO: 3 including one to seven repeats of the hexameric sequence represented in SEQ ID NO: 1, or (iii) a peptide fragment consisting essentially of one to seven repeats of the hexameric sequence represented by SEQ ID NO: 1, wherein said elastin-based composition is attached to a biocompatible support or dissolved in a biocompatible matrix and has one or more biological activities selected from the group consisting of:

- a) inhibiting the proliferation of smooth muscle cells;
- b) stimulating the differentiation of smooth muscle cells;
- c) regulating the migration of smooth muscle cells; and
- d) binding to smooth muscle cells, and

wherein said elastin-based composition has an IC₅₀/EC₅₀ for at least one of said biological activities that is less than or equal to 10⁻³.

61. (New) The composition of claim 60, wherein said polypeptide consists essentially of (i) an amino acid sequence at least 95% identical to SEQ ID NO: 3, (ii) a bioactive fragment of SEQ ID NO: 3 that includes one to seven repeats of the hexameric sequence represented in SEQ ID NO: 1 or (iii) a peptide fragment consisting essentially of one to seven repeats of the hexameric sequence represented by SEQ ID NO: 1.

62. (New) The composition of claim 60, wherein said polypeptide consists essentially of (i) an amino acid sequence identical to SEQ ID NO: 3, (ii) a bioactive fragment of SEQ ID NO: 3 that includes one to seven repeats of the hexameric sequence represented in SEQ ID NO: 1, or (iii) a peptide fragment consisting essentially of one to seven repeats of the hexameric sequence represented by SEQ ID NO: 1.

63. (New) The composition of claim 60, wherein said bioactive fragment or peptide fragment includes one repeat of the hexameric sequence represented in SEQ ID NO: 1.

64. (New) The composition of claim 60, wherein said bioactive fragment or peptide fragment includes two repeats of the hexameric sequence represented in SEQ ID NO: 1.

65. (New) The composition of claim 60, wherein said bioactive fragment or peptide fragment consists essentially of one repeat of the hexameric sequence represented in SEQ ID NO: 1.

66. (New) The composition of claim 60, wherein said bioactive fragment or peptide fragment consists essentially of two repeats of the hexameric sequence represented in SEQ ID NO: 1.

67. (New) A pharmaceutical composition that provides an elastin-based composition, said elastin-based composition consisting essentially of a polypeptide, wherein said polypeptide consists essentially of (i) an amino acid sequence at least 90% identical to SEQ ID NO: 3, (ii) a bioactive fragment of SEQ ID NO: 3 that includes one to seven repeats of the hexameric

sequence represented in SEQ ID NO: 1, or (iii) a peptide fragment consisting essentially of one to seven repeats of the hexameric sequence represented by SEQ ID NO: 1, wherein said elastin-based composition is attached to a biocompatible support or dissolved in a biocompatible matrix and has one or more biological activities selected from the group consisting of:

- a) inhibiting the proliferation of smooth muscle cells;
- b) stimulating the differentiation of smooth muscle cells;
- c) regulating the migration of smooth muscle cells; and
- d) binding to smooth muscle cells, and

wherein said elastin-based composition has an IC₅₀/EC₅₀ for at least one of said biological activities that is less than or equal to 10⁻³.

68. **(New)** The composition of claim 67, wherein said polypeptide consists essentially of (i) an amino acid sequence at least 95% identical to SEQ ID NO: 3, (ii) a bioactive fragment of SEQ ID NO: 3 that includes one to seven repeats of the hexameric sequence represented in SEQ ID NO: 1, or (iii) a peptide fragment consisting essentially of one to seven repeats of the hexameric sequence represented by SEQ ID NO: 1.

69. **(New)** The composition of claim 67, wherein said polypeptide consists essentially of (i) an amino acid sequence identical to SEQ ID NO: 3, (ii) a bioactive fragment of SEQ ID NO: 3 that includes one to seven repeats of the hexameric sequence represented in SEQ ID NO: 1, or (iii) a peptide fragment consisting essentially of one to seven repeats of the hexameric sequence represented by SEQ ID NO: 1.

70. **(New)** The composition of claim 67, wherein said bioactive fragment or peptide fragment consists essentially of one repeat of the hexameric sequence represented in SEQ ID NO: 1.

71. **(New)** The composition of claim 67, wherein said bioactive fragment or peptide fragment consists essentially of two repeats of the hexameric sequence represented in SEQ ID NO: 1.

72. **(New)** The composition of claim 60 or 67, wherein said bioactive fragment or peptide fragment consists essentially of six repeats of the hexameric sequence represented in SEQ ID NO: 1.

73. **(New)** The composition of claim 60 or 67, wherein said bioactive fragment or peptide fragment consists essentially of seven repeats of the hexameric sequence represented in SEQ ID NO: 1.